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| <b>HAMILTON, BROOK,<br/>SMITH &amp; REYNOLDS</b> | <b>FILING DATE</b> | <b>FIRST NAMED INVENTOR</b> | <b>ATTORNEY DOCKET NO.</b> |
|--|--------------------|-----------------------------|----------------------------|

07/991,997 12/17/92 BEACH

18N1/0714

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TWO MILITIA DRIVE  
LEXINGTON, MA 02173

D CSHL91-02AAA  
**EXAMINER**

HOUTTEMAN, S

|                 |                     |
|-----------------|---------------------|
| <b>ART UNIT</b> | <b>PAPER NUMBER</b> |
|-----------------|---------------------|

1807

DATE MAILED:

07/14/93

This is a communication from the examiner in charge of your application.  
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 4/9/93 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), — days from the date of this letter.  
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

**Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:**

- |   |  |
|---|--|
| 1. <input checked="" type="checkbox"/> Notice of References Cited by Examiner, PTO-892. | 2. <input checked="" type="checkbox"/> Notice re Patent Drawing, PTO-948.        |
| 3. <input checked="" type="checkbox"/> Notice of Art Cited by Applicant, PTO-1449.      | 4. <input type="checkbox"/> Notice of Informal Patent Application, Form PTO-152. |
| 5. <input type="checkbox"/> Information on How to Effect Drawing Changes, PTO-1474.     | 6. <input type="checkbox"/>  |

**Part II SUMMARY OF ACTION**

1. ☒ Claims 1-9 are pending in the application.  
Of the above, claims — are withdrawn from consideration.
2. ☐ Claims — have been cancelled.
3. ☐ Claims — are allowed.
4. ☒ Claims 1-9 are rejected.
5. ☐ Claims — are objected to.
6. ☐ Claims — are subject to restriction or election requirement.
7. ☐ This application has been filed with Informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on —. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on — has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on — has been ☐ approved. ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received  
☐ been filed in parent application, serial no. —; filed on —.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

15. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

16. Claims 1-9 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to the detection of cell transformation in tissue culture. See M.P.E.P. §§ 706.03(n) and 706.03(z).

Claims 1-9 read on the detection of transformation of all cell types in all tissues in vivo. Knowledge of p21, p16 and p19 and their interactions with cyclin and cyclin kinases is limited. The specification states, "The molecular identity of p21 is presently unknown (Specification p. 18, lines 8-9)," and specification contains no information about the molecular identity of p16 or p19. Also, ". . . the experimental techniques used in this study do not formally allow a distinction between the existence of multiple pair-wise interactions between each protein . . . [and] . . . a quaternary complex (Specification p. 20, lines 1-5). In addition, all the examples in the specification use tissue culture cells. It is well known that tissue culture conditions are not the same as in vivo conditions. It is possible that these proteins are associated differently in vivo or are expressed in much lower levels in some tissues. It

would require undue experimentation to develop protocols in which the claimed method could be used in vivo on all tissues.

17. Claims 1-9 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims are drawn to methods of diagnosis but recite no positive method steps. Without these steps it is not possible to determine what types of diagnostic methods are being claimed. Amendment to recite the steps in the examples in the specification is suggested.

18. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant

is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

19. Claims 1-9 are rejected under 35 U.S.C. § 103 as being unpatentable over Xiong et al. (Cell 71(3):504-14 Oct 30 1992).

Claims 1-3, 4-6 and 7-9 are drawn to a method of diagnosing transformation of a cell by determining if p21 is not complexed with cyclin, cyclin kinase or both. Claims 4-6 differ from 1-3 to recite a method of determining if p16 is complexed with cyclin or cyclin kinase. Claims 7-9 differ from 1-6 to recite a method of determining if p19 is complexed with cyclin. Claims 2, 3, 5, 6, 8 and 9 further limit their respective base claims to recite the use of an antibody and wherein the cyclin is a D-type cyclin or an A-type cyclin and wherein the cyclin kinase is CDK4.

Xiong et al. teaches a method detecting Cyclin D1 and cyclin kinase CDK5 associated with p21 only in transformed cells (see Xiong et al. Fig 1., Fig 2 and Fig. 7); using an antibody (see Xiong et al. Fig. 1). Xiong also teaches that CDK2 is associated with cyclin A (Xiong et al. p. 505, lines 12-14). Xiong et al. does not teach p16 or p19. However, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use the method of Xiong et al. on transformed cells and detect p16 and p19 because, using the Innunoprecipitation-Western blotting techniques taught by Xiong et al. these protein band would have appeared on the blots of

Serial No. 07/991,997  
Art Unit 1807

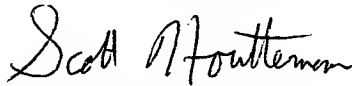
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Xiong just below the p21 band of Figure 1 in the extracts from transformed cell lines.

20. Papers relating to this application may be submitted to Group 180 by facsimile transmission. Papers should be faxed to Group 180 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax center numbers are (703) 305-3014 or (703) 308-4227.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott Houtteman whose telephone number is (703) 305-3394.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.



Scott Houtteman  
July 12, 1993

MARGARET MOSKOWITZ *PMR*  
SUPERVISORY PATENT EXAMINER  
GROUP 180